

REMARKS

The Office Action of April 1, 2010, presents the examination of claims 1, 4-6, 19, 29, 30 and 40, claims 7-18, 20-28, 31-34 and 39 being withdrawn from consideration following restriction and/or election of species.

Claim 1 is amended to recite that the invention resides in a composition of matter, and conforming amendments are made to all the pending claims as necessary. Claim 1 is also amended to delete reference to two yeast species from the Markush group of bacterial species. An additional minor editorial amendment is made to correct grammar and a misspelling in claims 32 and 34.

Rejections under 35 USC § 112, second paragraph

The Examiner rejects claims 1, 4-6, 19, 29, 30 and 40 under 35 USC § 112, second paragraph as being indefinite. The Examiner asserts that the phrase "micelles comprising exopolysaccharide" is somehow indefinite.

First, the language "micelles comprising exopolysaccharide" is not indefinite. Rather the phrase rather clearly indicates, in accord with common claim interpretation, a micelle that is composed of an exopolysaccharide and can include other ingredients. Nonetheless, claim 1 is amended to recite "exopolysaccharide micelles comprising an exopolysaccharide..." to assure the Examiner that the micelles are indeed formed of an exopolysaccharide material.

The Examiner further asserts that claim 1 has omitted some essential element, in that there is no recitation of a hydrophilic and a hydrophobic moiety, and a micelle is known to contain both.

First, the Examiner has admitted that a micelle is known to be formed from a material that has both a hydrophilic and a hydrophobic moiety. Thus, these characteristics of a micelle are implicit. Second, notwithstanding the Examiner's opinion, the present specification demonstrates by an experimental example (Example 5, beginning on page 12) that the EPS obtained from the bacterial strains of the claims, either as a consortium or as purified strains, forms micelles. Thus, there is no "essential component" missing from the phrase "exopolysaccharide micelles comprising exopolysaccharide produced by a bacterium selected from the group of bacteria consisting of *Lactobacillus* strain R2C2, *Lactobacillus* strain Inix,

Lactobacillus strain Esl, *Lactobacillus* strain K2...". Accordingly, the instant rejection should be withdrawn.

The Examiner also indicates that claim 1 includes within the recited Markush group microorganisms that are both bacteria and yeasts, and, since the claim recites "bacteria selected from the group consisting of...", the recited yeast species should be deleted. Claim 1 is so amended, thus obviating this rejection.

Finally, the Examiner indicates that claim 1 recites a "delivery system" and that it is therefore unclear which statutory class the invention falls into. All of the claims are amended to recite a "composition", thus obviating this ground of rejection.

Rejection for anticipation

Claims 1, 4-6, 19, 29 and 30 are rejected under 35 USC § 102(c) as lacking novelty over Simard '131. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants hereby note that the reference is not "by another" and provide the Declaration under 37 CFR 1.132, signed by Ms. Josée Beaulieu that attests to this fact. Thus, the instant rejection should be withdrawn.

Rejections for obviousness

Claims 1, 4-6, 19, 29, 30 and 40 are rejected under 35 USC § 103(a) as being unpatentable over Simard '131 in view of Campbell '392. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Simard '131 is not a prior art reference to the present application, and Campbell '392 is cited only for disclosure that a therapeutic agent can be incorporated into a liposome. Thus, the instant rejection cannot be sustained by reference to Campbell '392 alone and must be withdrawn.

Claims 1, 4-6, 29, 30 and 40 are also rejected under 35 USC § 103(a) as unpatentable over Abraham, Micheli, Maeda, Jolly and Campbell '392. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20

USPQ2d 1438 (Fed. Cir. 1991). Furthermore, a claim composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *KSR Int'l Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). There must be a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *Id.* Furthermore, there must be a reasonable expectation of success in making the invention. *In re Vaeck*. Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *KSR Int'l Co. v Teleflex Inc.*

Applicants submit that the Examiner has failed to establish *prima facie* obviousness of the invention from the collection of references cited. The Examiner has only selected elements disclosed in the cited art without even considering why a person skilled in the art should combine these references and whether such combination will indeed produce the claimed invention. Further, none of the cited art teaches EPS micelles as claimed herein, and therefore the collection of them fails to disclose or suggest every element of the claims.

Abraham et al. only teaches fermenting cow's milk with kefir grains. Nowhere in Abraham is there discussed, taught or even suggested the production of EPS micelles following fermentation with kefir grain. The Examiner relies on Abraham to provide evidence that *Lactobacillus* species are known and that they are present in kefir grains in a matrix that includes proteins and polysaccharides. But as acknowledged by the Examiner, the particular strains of *Lactobacillus* R2C2, INIX, ES1 and K2 as recited in the claims are not disclosed by Abraham.

The Examiner adds Micheli for disclosure that kefir grains include a branched heteropolysaccharide and Maeda for disclosure that the branched heteropolysaccharide has a molecular weight of about 760 kDa. Applicants submit that neither of Micheli nor Abraham adds anything further to the disclosure of Abraham, and certainly neither of these two references disclose either that micelles can be formed from the EPS produced by lactobacilli, nor that the particular species of lactobacilli recited in the claims should be selected.

Jolly is cited for teaching that EPS synthesized by lactobacilli have therapeutic effects in treatment of cancers, and Campbell '392 is cited for incorporation of taxane drugs into liposome formulations. However, once again neither of these references discloses the formation of

micelles from bacterial EPS, nor that the particular lactobacilli recited in the claims should be selected.

Thus, the collection of references cited in the first instance fails to disclose or suggest each and every recitation in the claims, and furthermore fails to establish any expectation of success in making the invention in one of ordinary skill in the art who reads the collection of references. Accordingly, the Examiner has failed to establish *prima facie* obviousness of the claimed invention and the instant rejection should be withdrawn.

The Examiner complains that the USPTO has no way to determine whether the EPS produced by the lactobacilli recited in the claims is different from that produced by the lactobacilli of Abraham or Maeda. Abraham teaches the use of kefir grains. Maeda teaches the use of ATCC 43761, a *Lactobacillus kefirano-faciens* strain.

Applicants provide below data showing differences in the sugar fermentation profile of the four strains recited in the claims, R2C2, INIX, K2, ES1, and also of ATCC 43761, *i.e.* the strain of reference for *Lactobacillus kefirano-faciens*, and several *Lactobacillus kefirano-faciens* and *Lactobacillus kefirgranum* strains (that is, the lactobacilli found in kefir grains) that are described in Fujisawa et al. and Vancanneyt et al. These data suffice to establish the differences between these strains as follows:

Table 1: Sugar fermentation profile of several strains.

Substrate	R2C2	INIX	K2	ES1	ATCC 43761	Fujisawa et al., 1988.	Vancanneyt et al., 2004. <i>Kefirano-faciens</i>	Vancanneyt et al., 2004. <i>L. Kefirgranum</i>
Number of experiments	4	2	3	3	3			
Glycerol							-	-
Erythritol							-	-
D-Arabinose						-	-	-
L-Arabinose							-	-
Ribose							-	-
D-Xylose						-	-	-
L-Xylose							-	-
Adonitol							-	-
β-Methyl xyloside							-	-
Galactose						+	+	+

Substrate	R2C2	INIX	K2	ESI	ATCC 43761	Fujisawa et al., 1988.	Vancannet et al., 2004. <i>Keffirano-faciens</i>	Vancannet et al., 2004. <i>L.Keffirgranum</i>
D-Glucose						+	+	+
D-Fructose						+	+	+
D-Mannose						+/-	-	-
L-Sorbose							-	-
Rhamnose						-	-	-
Dulcitol							-	-
Inositol							-	-
Mannitol						-	-	-
Sorbitol						-	-	-
α -Methyl-D-Mannoside							-	-
α -Methyl-D-Glucoside							-	-
N-acetyl glucosamine							+/-	+/-
Amygdaline						-	-	+/-
Arbutine							-	+/-
Esculine						-	-	+
Salicine						-	-	++/-
Cellobiose						-	-	+/-
Maltose						+	+/-	+
Lactose						+	+	+
Melibiose						+	+/-	+
Sucrose						+	+	++/-
Trehalose						-	-	++/-
Inuline							-	+/-
Melezitose						-	-	-
D-Raffinose						+	+/-	++/-
Amidon						-	-	-
Glycogene							-	-
Xylitol							-	-
β -Gentibiose							-	+/-
D-Turanose							-	+/-
D-Lyxose							-	-
D-Tagarose							-	-
D-Fucose							-	-
L-Fucose							-	-

Substrate	R2C2	INIX	K2	ESI	ATCC 43761	Fujisawa et al., 1988.	Vancanneyt et al., 2004. <i>Keffranofaciens</i>	Vancanneyt et al., 2004. <i>L.Keffranum</i>
D-Arabitol							-	-
L-Arabitol							-	-
Gluconate							-	-
2-ceto-gluconate							-	-
5-ceto-gluconate							-	-

■ strong ■ medium ■ light

+/- = strain dependant

++/- = almost all the strains

Copies of the Fujisawa et al. (1988) and Vancanneyt et al. (2004) references, as well as Takizawa et al. (1994) cited in Vancanneyt's title, are attached for the Examiner's convenience.

Applicants also provide here additional information showing that the strains have physical differences (see Table 2).

Table 2 : Comparison of different strains from *L. keffranofaciens* species.

Strain	Characteristics
R2C2	<ul style="list-style-type: none"> ◆ Bacillus of short length, medium thickness, producing few or no exopolysaccharides. ◆ Length and thickness of the bacilla vary according to the culture medium used and the conservation medium used before subculturing. ◆ Typical colonies : white with beige in the center, convex, embossed on surface, smooth and glittering. ◆ Very robust strain: good growth in minimal media, for instance not supplemented in whey. ◆ Strain selected for the industrial production of MPM. ◆ Rarely presents agglomerates of small size in culture (about 10 bacteria or less). ◆ Does not promote formation of agglomerates of proteins during production of MPM.
INIX	<ul style="list-style-type: none"> ◆ Longer and thinner bacilla. ◆ Colonies are viscous looking. ◆ Strain slightly robust, very slow growth in minimal media. ◆ Products producing exopolysaccharides in high quantities in RCW medium ◆ Occasionally presents agglomerates of small and medium size (about 10 to 50 bacteria). ◆ Cells are entrapped in the protein matrix during production of MPM.
ESI	<ul style="list-style-type: none"> ◆ Similar to R2C2 strain, but showing a less good growth in minimal media.

Strain	Characteristics
K2	<ul style="list-style-type: none">◆ Bacilla of average length, slightly thicker than R2C2.◆ Produces few or no exopolysaccharides.◆ Growth in minimal media, but reaching the stationary phase at a level lower than other strains in every media (RCW : 5 to 7 X 10⁸ bacteria compared to 1.5 to 3 X 10⁹ for R2C2 and ES1).◆ Shows agglomerates of medium size (about 50 to 100 bacteria).
ATCC 43761	<ul style="list-style-type: none">◆ Weak production of exopolysaccharides.
ATCC 51647	<ul style="list-style-type: none">◆ Bacilla of medium length, thicker than every other strain, producing few or no exopolysaccharides. Irregular surface of the cells.◆ White colonies, convex, with a more uniform top, but showing some fine white points on the surface.◆ Growth in minimal media, but strongly reduced in presence of high concentration of calcium (1% CaCl₂ w/v).◆ Always presents agglomerates of higher size also containing precipitated proteins (more than 100 bacteria).◆ Always promotes the formation of agglomerates with proteins during the production of MPM.

Therefore, in the absence of evidence to the contrary provided by the Examiner, Applicants submit that the strains recited in claim 1 are not disclosed or suggested by Abraham, Micheli, or Maeda, all of which disclose bacteria obtained from kefir grain.

Claims 1, 4-6, 19, 29, 30 and 40 also stand rejected under 35 USC 103(a) as being unpatentable over Hartkorn, Micheli, Maeda, Jolly and Campbell '392. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants submit that the Examiner again fails to establish *prima facie* obviousness of the claimed invention. The deficiencies of Micheli et al., Maeda et al., Jolly et al. and Campbell '392 in failing to disclose elements of the invention or to establish an expectation of success in making the invention are set forth above. The substitution of Hartkorn for Abraham as the primary reference does not remedy the failure of the whole collection of references to establish *prima facie* obviousness of the invention.

Hartkorn only describes using kefir microorganisms in a method for removing pathogenic germs and dissolved organic substances from liquids. Specifically, kefir milk bacteria are added to the liquid where they will take up the germs after multiple passages through the column. Hartkorn is more concerned about degradation of germ proteins than formation of micelles. The Examiner emphasizes that Hartkorn produces a spherical coherent culture.

A spherical coherent culture is not an indication that micelles are produced. That is, not all spherical structures suspended in a liquid constitute micelles. For example, fat droplets suspended in water are also spherical, but differ substantially from micelles.

Thus, disclosure by Hartkorn that a spherical droplet of a bacterial culture is formed does not at all suggest formation of micelles (or of liposomes) of an exopolysaccharide material. Thus, like Abraham, Hartkorn does not teach or even suggest that micelles of EPS produced by a bacterium selected from the group consisting of *Lactobacillus* strain R2C2, *Lactobacillus* strain INIX, *Lactobacillus* strain ES1, and *Lactobacillus* strain K2 can or should be made.

Accordingly, the collection of Hartkorn, Micheli, Maeda, Jolly and Campbell '392 fails to establish *prima facie* obviousness of the present invention and the rejection of claims 1, 4-6, 19, 29, 30 and 40 as obvious over these references should be withdrawn.

Claims 1, 4-6, 19, 29, 30 and 40 are also rejected under 35 USC 103(a) as being obvious in view of Hori, Micheli, Maeda, Jolly and Campbell '392. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Yet again the Examiner fails to establish *prima facie* obviousness of the present invention. As above, the deficiencies of Micheli et al., Maeda et al., Jolly et al. and Campbell '392 in failing to disclose elements of the invention or to establish an expectation of success in making the invention are previously set forth. The substitution of Hori for Abraham as the primary reference does not remedy the failure of the whole collection of references to establish *prima facie* obviousness of the invention.

As a threshold matter, Applicants wish to point out that the instant rejection is one made for obviousness, not anticipation, and therefore the Examiner's suggestion of inherent anticipation by Hori is confusing.

However, in regard to the substance of the rejection, Applicants first assert that for a result to be inherent, it must necessarily arise from the conditions precedent established in the reference cited. It is insufficient to establish inherency that the result might result from those conditions, or even that it is a probable result. See, e.g. *Ex parte Vander Wal and Van Akkeren*, 109 USPQ 119 (BPAI 1955); *In Hansgirk v. Kemmer*, 40 USPQ 665, 667 (CCPA 1939). Furthermore, the precipitation of an aggregate of microorganisms and proteins is manifestly not the same as formation of a micelle.

Hori describes a process for producing a lactic acid drink. The Examiner acknowledges that, at most, Hori teaches the production of whey and a precipitate which comprises microorganisms and insoluble proteins. Nowhere in Hori is the production of EPS micelles produced by a bacterium selected from the group consisting of *Lactobacillus* strain R2C2, *Lactobacillus* strain INIX, *Lactobacillus* strain ES1, and *Lactobacillus* strain K2, described or suggested.

Again, the collection of references cited completely fails to disclose or suggest at least two recitations in the present claims (formation of micelles from EPS and selection of the lactobacillus species listed). Indeed, although the Examiner asserts formation of micelles from EPS is obvious in view of the references, the Examiner fails to say where this recitation is present in the references.

Finally, in regard to all of the rejections based for obviousness, the instant invention might be viewed as presenting results not expected by one of ordinary skill in the art who reads the references collected by the Examiner. That is, in making the rejection based upon indefiniteness, the Examiner asserts that one of ordinary skill in the art would not understand that micelles could be formed from EPS from lactic acid bacteria absent inclusion also of a hydrophobic moiety in the EPS. Yet, the present specification includes evidence (Example 5) that indeed micelles can be obtained from EPS prepared from the recited lactobacilli. Accordingly, this result can be considered unexpected by one of ordinary skill in the art who reads the references cited by the Examiner, and sufficiently so that it would overcome any case of *prima facie* obviousness that might be deemed established by those references.

Obviousness-type double patenting

Claims 1, 4-6, 29, 30 and 40 are provisionally rejected under the doctrine of obviousness-type double patenting over claims 1, 2, 5, 12-14, 16-18, 27-29 53, 70-74 and 76-79 of copending application 10/499,313 in view of Campbell '392. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants point out that the inclusion of the Campbell '392 reference for disclosure of an element of the claims in support of a rejection for obviousness-type double patenting, rather than only as evidence of the interpretation of the terms of the claims, is legal error. A rejection for

obviousness-type double patenting is properly based only upon the claims of the underlying application or patent asserted in making the rejection.

Notwithstanding the legal error of the Examiner, Applicants note the provisional nature of the rejection and will address it substantively (if it is made properly) when claims in one or the other application are found to be otherwise allowable.


Applicants submit that the present claims recite subject matter patentable over the prior art of record. The favorable actions of allowance of claims 1, 4-6, 29, 30 and 40, and rejoinder of claims 7-28 under election of species practice, and of claims 31-34 and 39 pursuant to MPEP 821.04 are requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. (Reg. No. 36,623) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: September 30, 2010

Respectfully submitted,

By 
Mark J. Nuell, Ph.D.
Registration No.: 36,623
BIRCH, STEWART, KOLASCH & BIRCH, LLP
12770 High Bluff Drive, Suite 260
San Diego, California 92130
(858) 792-8855
Attorney for Applicant

Attachments:

Josée Beaulieu 1.132 Declaration
Fujisawa et al. (1988)
Vancanneyt et al. (2004)
Takizawa et al. (1994)